GROWTH CURVES FOR BODY WEIGHT OF THE LABORATORY RAT*

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Body weight growth of rats, bred and reared in small cages, occurs in two main stages, which overlap to a degree. During the first stage, when rats develop to maturity, all parts of the animal (e.g. head, body, limbs, tail) grow, resulting in high relative growth rates. During the second stage, one of post-maturity growth, there is an increase in body weight, unaccompanied by corresponding significant changes in such measures as limb and tail length. It is thought that the increase in body weight during the second stage is due to an increase in body fat; however, further experimentation is required to verify this contention.

This note is an initial step in a detailed study of the extent and nature of body weight growth in rats reared in small cages. Interest is centred on the first stage of growth, when it seems reasonable to assume that body weight can be represented mathematically as a function of time. From the fitted growth functions, values of the absolute and relative growth rates were computed; also, preliminary information concerning the extent of the two stages of growth is obtained. It is hoped that by further experimentation involving (1) measurement of limb and tail lengths (measures largely independent of body fat content), and (2) provision of exercising periods (to offset lack of exercise in the cages), a more complete description of body weight growth can be obtained.

A detailed knowledge of body weight growth is of important application to the use of rats for the screening of drugs. As many drugs are absorbed by fats to varying degrees, it is often desirable to ensure rats have a minimum of body fat in order to obtain reliable comparisons of the potencies of different drugs.

Experimental Data

The source of data was a collection of litters, born between February 24 and March 1, 1966, at the Division of Animal Health, CSIRO, Parkville, Vic. Weaning was completed by March 28, when all rats were weighed. One male and one female were selected randomly from each of 10 litters, after exclusion of obvious "runts". Each group of 10 rats of the same sex was then divided into two subgroups of 5, and all rats of a subgroup were placed in a cage of dimensions 14·5 by 11·5 in. and 9·5 in. deep. The animals were weighed at weekly intervals for approximately 14 months. Food and water were freely available to all animals throughout the experiment.

The food used for this experiment was a commercially produced dog food, in the form of cubes. Chemical analysis showed that the crude fat content of this food was 4–7%. Thus the diet could be regarded as one of low fat content.

Growth Curves

Plots of the body weight against time are presented in Figure 1. Only those body weights are plotted for the period over which growth curves were fitted. Also plotted in Figure 1 are the mean body weights of groups of males and females at age 7, 14, and 21 days, as recorded in another experiment. As a different method of choice

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of these groups was used (more than one rat from each litter), the supplementary data was not used in the computation of the growth curves. Hence the supplementary points in Figure 1 are plotted in different symbols (open circles and triangles).

It is evident on examination of Figure 1 that a sigmoidal (S-shaped) function is required to adequately represent body weight as a function of time during the period plotted; that separate growth curves are required for males and females, as the difference between males and females steadily increases from approximately 30 days of age.

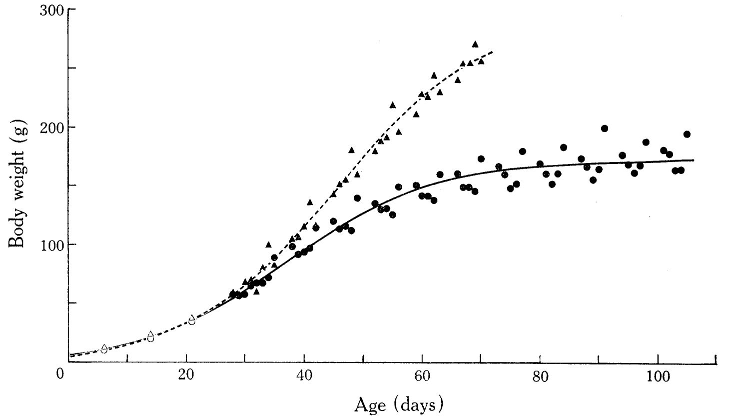

Fig. 1.—Relationship between body weight and age for male (▲, △) and female (●, ○) laboratory rats. Open symbols have been used for supplementary data (see text). ——— Female line; – – – – male line.

It was found that a logistic curve of body weight on time gave an adequate fit for males to age 70 days, and for females to age 105 days. No function was found to fit the entire data (i.e. over 14 months) satisfactorily, probably because of the complex nature of body weight growth as outlined previously. The periods, over which growth curves were fitted (70 days for males and 105 days for females) were determined empirically by fitting a logistic curve to successively larger periods until the fit was no longer adequate, as judged by examining plots of observed and predicted body weights. As the purpose of fitting growth curves was primarily for computing absolute and relative growth rates, it was considered sufficient to fit a single curve to the data of all animals of one sex rather than fit separate curves for each animal. Alternative forms of sigmoidal function (e.g. Gompertz double exponential) did not give significantly different conclusions.

If the functional relationship between body weight and time is logistic, then

$$y = K/[1+\exp(\alpha-\beta t)], \tag{1}$$

where y = body weight, t = time, and K, α, and β are constants with K and β necessarily positive. This relationship may be rewritten as

$$1/y = A+B\exp(-\beta t), \tag{2}$$

where $A = 1/K$, and $B = \exp(\alpha/K)$, in which form curve-fitting is computationally easier because the number of non-linear constants is reduced to one (viz. β).

The resultant fitted equations, in form (2), obtained by non-linear regression analysis were

$$\text{Males:}\qquad 1/y = 0\cdot003407+0\cdot1409\exp(-0\cdot082t),$$

$$\text{Females:}\qquad 1/y = 0\cdot005800+0\cdot1248\exp(-0\cdot082t).$$

Rearranging these equations in that of form (1), they may be written

$$\text{Males:}\qquad y = 293\cdot5/[1+\exp(3\cdot722-0\cdot082t)],$$

$$\text{Females:}\qquad y = 172\cdot4/[1+\exp(3\cdot069-0\cdot082t)].$$

Growth curves computed from these latter equations have been drawn in Figure 1.

It would be premature to attach too much biological significance to the parameters estimated in these equations. The limiting values (for large t) for body weight, as given by the fitted curves, are 293·5 g for males and 172·4 g for females. As the observed mean body weights at 14 months were 485 g for males and 264 g for females, it is obviously invalid to extrapolate predicted body weights beyond 70 days for males and 105 days for females. However, from Figure 1, it can be seen that the observed body weights at 7, 14, and 21 days are in close agreement with predictions; thus it is probably reasonable to extrapolate for the period 0 to 28 days.

Table 1

ABSOLUTE AND RELATIVE GROWTH RATES FOR MALE AND FEMALE RATS AT DIFFERENT AGES

Absolute growth rates given as grams per day, and relative growth rates as a percentage of body weight

Age (days)	Male Growth Rate		Female Growth Rate	
	Absolute	Relative	Absolute	Relative
7	1·0	7·9	1·0	7·6
14	1·6	7·6	1·6	7·1
21	2·5	7·2	2·3	6·5
28	3·8	6·6	3·1	5·6
35	5·0	5·7	3·5	4·5
42	5·9	4·6	3·4	3·3
49	5·9	3·5	2·8	2·3
56	5·0	2·4	2·1	1·5
63	3·7	1·6	1·4	0·9
70	2·5	1·0	0·9	0·5

Absolute and Relative Growth Rates

If the body weight is a known function of time, say $y(t)$, then absolute growth rate at time $t = t_1$ is $[\mathrm{d}y(t)/\mathrm{d}t]_{t=t_1}$; relative growth rate at time $t = t_1$ is $y(t)^{-1}[\mathrm{d}y(t)/\mathrm{d}t]_{t=t_1}$, where $[\mathrm{d}y(t)/\mathrm{d}t]_{t=t_1}$ means "the derivative of $y(t)$ with respect to t, evaluated at $t = t_1$". Applying these formulas to the growth functions, given previously for nominated ages, values for absolute and relative growth rates were obtained as given in Table 1.

Discussion

It may be thought that growth curve analysis is an unnecessarily complicated way of determining growth rates. The following simple alternative may be thought preferable. If the weights of n rats are W_{1i} and W_{2i} ($i = 1, 2, \ldots, n$) at successive times t_1 and t_2 respectively, then an estimate of absolute growth rate over the period between t_1 and t_2 is equal to

$$\sum_{i=1}^{n} (W_{2i}-W_{1i})/[n(t_2-t_1)].$$

An equally simple formula can be given for relative growth rate. It was found that growth rates calculated by these simple methods did not differ markedly from those given in Table 1. However, the simple method assumes a linear growth between t_1 and t_2, and utilizes only the data on body weight for the particular time interval of interest. Growth curve analysis does not require an assumption of linear growth within small time intervals, and utilizes all the data simultaneously. A more important reason for preferring growth curve analysis in the experimental situation described above is that it provides a basis for describing a comprehensive model of body weight growth.

On fitting the logistic curve to body weights, it was found that (1) a satisfactory fit could be obtained for males to age 70 days, but for females to age 105 days; (2) in the formulas for body weight growth the coefficient of t (the time variate) in the exponent was the same for males and females (viz. $-0 \cdot 082$). Until more complete information is available regarding body weight growth, little biological significance can be attached to these results.

An examination of the absolute and relative growth rates of Table 1 is of interest. The relative growth rate for females at age t days is the same as the relative growth rate for males at age $(t+7)$ days. Thus the relative growth patterns for males and females are similar, the difference being that they are 1 week out of phase. As a consequence, the maximum absolute growth rate occurs a week earlier for females (at approximately 38 days) than for males (approximately 45 days), but the values of the maxima differ ($3 \cdot 5$ g/day for females *v.* $5 \cdot 9$ g/day for males).

In conclusion, it is contended that many useful facts about body weight growth have been introduced, and that a basis for planning a more comprehensive study of body weight growth has been established.

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